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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/981,998	05/11/1998	STEFAN M. PULST	232.00010120	8733

7590 10/01/2002

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EXAMINER
GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/01/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/981,998	Applicant(s) PULST, STEFAN M.	
	Examiner Jeanine A Goldberg	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/5/002; 9/3/02* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,7,59,61,71-73,75 and 82-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *59,61,71-73 and 75* is/are allowed.

6)☒ Claim(s) *1-3,5,7 and 82-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed March 5, 2002 and September 3, 2002.

2. Currently, claims 1-3, 5, 7, 59, 61, 71-73, 75, 82-84 are pending. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. The instant claims were first presented March 5, 2002 and therefore, a final rejection is appropriate for the newly amended claims. This action is FINAL.

3. Any objections and rejections not reiterated below are hereby withdrawn.

4. This action contains new grounds of rejection necessitated by amendment.

Priority

5. The examiner notes that the response asserts that certain parts of certain sequences are deemed earlier priority dates. For the purpose of clarity, the sequences which are found in the pending claims are provided the following priority dates.

6. It is noted that SEQ ID NO: 19 has been added from the parent application. SEQ ID NO: 19 appears to contain only about 400 amino acids from the 1135 amino acids of the full length mouse SCA2 polypeptide. Thus, SEQ ID NO: 19 appear to be a partial polypeptide for the full length mouse SCA2 polypeptide. While SEQ ID NO: 19 appears to have priority to October 8, 1996, a claim drawn to a nucleic acid encoding a full length SCA2 polypeptide is enabled only as of May 8, 1997 when the full length mouse polypeptide was described.

SEQ ID NO: 1 nucleotides 1-516	October 8, 1996
SEQ ID NO: 2 nucleotides 163-4098 (coding portion)	October 8, 1996
SEQ ID NO: 2 nucleotides 163-657 (5' coding portion)	October 8, 1996
SEQ ID NO: 2 nucleotides 724-4098 (3' coding portion)	October 8, 1996
SEQ ID NO: 4 nucleotides 50-3454 (coding portion)	May 8, 1997
SEQ ID NO: 4	May 8, 1997
SEQ ID NO: 5	May 8, 1997
SEQ ID NO: 6	May 8, 1996
SEQ ID NO: 7	May 8, 1996
SEQ ID NO: 19 (newly added from parent application)	October 8, 1996

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3, 7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to "isolated nucleic acid obtained from locus q24.1 of chromosome 12 of a human with symptoms of spinocerebellar ataxia, wherein the nucleic acid comprises an open reading frame encoding a polypeptide of greater than

140.1 kDa and a CAG repeat region comprising at least 35 repeats encoding a polyglutamine tract, or a recombinantly produced nucleic acid having the nucleotide sequence of the isolated nucleic acid."

The post filing date art teaches the genomic structure of the SCA2 on chromosome 12q24.1 (Sahba et al. Genomics, Vol. 47, pages 359-364, 1998). Sahba teaches a schematic of the SCA2 gene which contains 25 exons of variable length. Moreover, Sahba teaches all of the exon-intron boundaries and their corresponding sequence have been identified along with alternative splicing of one exon.

Choudhry et al. (Human Molecular Genetics. Vol. 10, No. 21, pages 2437-46, October 2001) teaches two novel SNPs which are in exon 1 of the SCA2 gene. The two SNPs form a haplotype which is associated with SCA2. Moreover, Mizushima et al. (J. of Medical Genetics. Vol. 36, No. 2, pages 112-114, February 1999) teaches detection of CCG or CCGCCG interruptions in expanded families.

The claims are drawn broadly to encompass the SCA2 genomic sequence. While the specification teaches [with respect to the 'SCA 2 gene'] "such nucleic acids can be obtained, for example, from human chromosome 12, specifically at the q24.1 locus, which is the site of mutations that cause SCA2" (page 10, lines 22-25), the q24.1 locus on chromosome 12 encompasses thousands of sequences, including sequences that would define the SCA2 gene such as regulatory sequences, introns, etc. that have not been taught or described in the specification. The incomplete disclosure of a "SCA2 gene" in the specification does not support the full scope of the claimed nucleic acid. While the specification asserts that DNA probes derived from the SCA2 gene could be

used to isolate a nucleic acid encoding an SCA2 polypeptide (p. 10, lines 30-35), the specification does not teach any probes derived from SCA2 genomic DNA nor does the specification teach the genomic DNA that the probes would be derived from. It is unclear what genomic sequences the term "gene" encompasses, for instance is such limited to only intronic sequences, or does it include 5' and 3' noncoding sequences, regulatory regions, etc. As stated previously, these sequences have not been taught by the specification. Further, while the specification teaches with regard to sequences that would be included in the SCA 2 gene "nucleic acids may include, but are not limited to, nucleic acids having substantially the same nucleotide sequence set forth in SEQ ID NO: 2" (page 11. lines 8-12), the specification does not define what is meant by 'substantially the same nucleotide sequence as..." such that the skilled artisan would be able to determine whether such recitation encompassed only the degeneracy of the genetic code, or also encompassed nucleotide polymorphisms or mutations that have not been taught in the specification.

As written the claims are broadly drawn to encompass genomic DNA, of which the instant specification has not described a full genomic sequence. Sahba et al provides that the genomic sequence contains 25 exons and introns and regulatory regions which are not described in the instant specification. Moreover, the claims are sufficiently broad to encompass a huge genus of nucleic acids which contain not only CAG repeat length variants, but also additional variants within the coding or intronic regions of the gene which have not been described. The post filing date art illustrates that the genus of nucleic acids encompassed by this claim includes SNPs and CCG

interruptions which have not been described in the instant application. The description of a single coding sequence, namely SEQ ID NO: 2 and variants of SEQ ID NO: 2 where in the variants are an isolated nucleic acid comprising a 5' coding sequence a CAG repeat region and a 3' coding sequence wherein the 5' coding region consists of nucleotides 163-657 of SEQ ID NO: 2; wherein the CAG repeat region consists of at least 35 CAG repeats; and wherein the 3' coding region consists of nucleotides 724-4098; wherein the 5' coding region is immediately upstream of the CAG repeat region which is immediately upstream of the 3' coding region does not provide description to the larger genus of nucleic acids. Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus of isolated nucleic acid obtained from locus q24.1 of chromosome 12 of a human with symptoms of spinocerebellar ataxia, wherein the nucleic acid comprises an open reading frame encoding a polypeptide of greater than 140.1 kDa and a CAG repeat region comprising at least 35 repeats encoding a polyglutamine tract, or a recombinantly produced nucleic acid having the nucleotide sequence of the isolated nucleic acid. As stated above, the genus encompasses not only the genomic sequence of the SCA2 gene, but also splice variants, polymorphism, mutations, insertions, deletions which have not been described at the time the invention was made.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-3, 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding SEQ ID NO: 3, does not reasonably provide enablement for any isolated nucleic acid obtained from locus q24.1 of chromosome 12 of a human with symptoms of spinocerebellar ataxia, wherein the nucleic acid comprises an open reading frame encoding a polypeptide of greater than 140.1 kDa and a CAG repeat region comprising at least 35 repeats encoding a polyglutamine tract, or a recombinantly produced nucleic acid having the nucleotide sequence of the isolated nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are broadly drawn to isolated nucleic acid obtained from locus q24.1 of chromosome 12 of a human with symptoms of spinocerebellar ataxia, wherein the nucleic acid comprises an open reading frame encoding a polypeptide of greater than 140.1 kDa and a CAG repeat region comprising at least 35 repeats encoding a polyglutamine tract, or a recombinantly produced nucleic acid having the nucleotide sequence of the isolated nucleic acid.

The claims are drawn broadly to encompass the SCA2 genomic sequence. While the specification teaches [with respect to the 'SCA 2 gene'] "such nucleic acids can be obtained, for example, from human chromosome 12, specifically at the q24.1 locus, which is the site of mutations that cause SCA2" (page 10, lines 22-25), the q24.1 locus on chromosome 12 encompasses thousands of sequences, including sequences

that would define the SCA2 gene such as regulatory sequences, introns, etc. that have not been taught or described in the specification. The incomplete disclosure of a "SCA2 gene" in the specification does not support the full scope of the claimed nucleic acid. While the specification asserts that DNA probes derived from the SCA2 gene could be used to isolate a nucleic acid encoding an SCA2 polypeptide (p. 10, lines 30-35), the specification does not teach any probes derived from SCA2 genomic DNA nor does the specification teach the genomic DNA that the probes would be derived from. It is unclear what genomic sequences the term "gene" encompasses, for instance is such limited to only intronic sequences, or does it include 5' and 3' noncoding sequences, regulatory regions, etc. As stated previously, these sequences have not been taught by the specification. Further, while the specification teaches with regard to sequences that would be included in the SCA 2 gene "nucleic acids may include, but are not limited to, nucleic acids having substantially the same nucleotide sequence set forth in SEQ ID NO: 2" (page 11. lines 8-12), the specification does not define what is meant by 'substantially the same nucleotide sequence as..." such that the skilled artisan would be able to determine whether such recitation encompassed only the degeneracy of the genetic code, or also encompassed nucleotide polymorphisms or mutations that have not been taught in the specification. As written the claims are broadly drawn to encompass genomic DNA, of which the instant specification has not described a full genomic sequence. Moreover, the claims are sufficiently broad to encompass a huge genus of nucleic acids which contain not only CAG repeat length variants, but also additional variants within the coding or intronic regions of the gene which have not been

described. The description of a single coding sequence, namely SEQ ID NO: 2 and variants of SEQ ID NO: 2 where in the variants are an isolated nucleic acid comprising a 5' coding sequence a CAG repeat region and a 3' coding sequence wherein the 5' coding region consists of nucleotides 163-657 of SEQ ID NO: 2; wherein the CAG repeat region consists of at least 35 CAG repeats; and wherein the 3' coding region consists of nucleotides 724-4098; wherein the 5' coding region is immediately upstream of the CAG repeat region which is immediately upstream of the 3' coding region does not provide description to the larger genus of nucleic acids. Accordingly, Applicants have not adequately taught the skilled artisan how to make the relevant identifying characteristics within the claimed genus of isolated nucleic acid obtained from locus q24.1 of chromosome 12 of a human with symptoms of spinocerebellar ataxia, wherein the nucleic acid comprises an open reading frame encoding a polypeptide of greater than 140.1 kDa and a CAG repeat region comprising at least 35 repeats encoding a polyglutamine tract, or a recombinantly produced nucleic acid having the nucleotide sequence of the isolated nucleic acid.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 5, 82-84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 5, 82-84 are directed to isolated nucleic acid wherein the isolated nucleic acid encodes a polypeptide of SEQ ID NO: 3 (5). The hybridization conditions of a complement of this nucleic acid is superfluous since the nucleic acid being claims is not the complement. In the event that the claims were amended to be directed to a complement which encodes SEQ ID NO: 3 (5), the claim would lack description. Moreover, as written Claims 5 and 72 are the same scope. Similarly, Claim 82 and 59 are of the same scope. Therefore, as written the claim does not particularly point out and distinctly claim the subject matter. Claims 83-84 are depended upon the independent claims.

Allowable Subject Matter

10. Claims 59, 61, 73 are allowable over the art. The prior art does not teach the SCA2 nucleic acid from the mouse which are SEQ ID NO: 4, 5, 19 (limitations of Claims 59 and 61).

11. Claims 71, 72, and 75 are directed to SCA2 nucleic acids of nucleotides 163-4098 of SEQ ID NO: 2, encoding the amino acid sequence of SEQ ID NO: 3, SEQ ID NO: 6-7 are allowable over the art. The art fails to teach an isolated nucleic acid comprising nucleotides 163-4098 of SEQ ID NO: 2; an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO: 3; an isolated nucleic acid comprising the nucleic acid sequence of SEQ ID NO: 19; a vector comprising an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO: 3.

In the event that Claims 1-3, 7 were cancelled, applicant may wish to file claims directed to the SCA2 nucleic acid with expanded number of repeats. For example, "An isolated nucleic acid comprising a 5' coding sequence a CAG repeat region and a 3' coding sequence wherein the 5' coding region consists of nucleotides 163-657 of SEQ ID NO: 2; wherein the CAG repeat region consists of at least 35 CAG repeats; and wherein the 3' coding region consists of nucleotides 724-4098 of SEQ ID NO: 2; wherein the 5' coding region is immediately upstream of the CAG repeat region which is immediately upstream of the 3' coding region."

Moreover, An isolated nucleic acid comprising a 5' coding sequence a CAG repeat region and a 3' coding sequence wherein the 5' coding region consists of a nucleic acid encoding amino acid residues 1-165 of SEQ ID NO: 3; wherein the CAG repeat region consists of at least 35 repeats; and wherein the 3' coding region consists of a nucleic acid encoding amino acid residues 187-1312 of SEQ ID NO: 3; wherein the 5' coding region is immediately upstream of the CAG repeat region which is immediately upstream of the 3' coding region."

Conclusion

12. Claims 59, 61, 71-73, 75 are allowable.

13. Claims 1-3, 5, 7, 82-84 are rejected.

14. Applicant's amendment in Paper Number 34, filed March 5, 2002 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of formal matters can be directed to the patent analyst, Pauline Farrier, whose telephone number is (703) 305-3550.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jeanine Goldberg
September 26, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600